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## Description

This invention is directed to a medically useful lyophilized sponge product having a density of 0.01 to 0.10 g/cm<sup>3</sup>.

Such a sponge product has been described in U.S. Patent No. 2,764,159 (Masci et al) but in that patent the product is based on a specified cellulose glycolic acid ether. Reference is made to similar gelatin-based products but these are stated to be less preferred and there is no reference to mixtures of hydrocolloids.

U.S. Patent No. 3,972,328 (Chen) discloses a surgical bandage of particular structure employing a pressure-sensitive adhesive layer including a pressure-sensitive rubbery elastomer adhesive material having intimately mixed therein a number of materials including a water-soluble or swellable hydrocolloid material or a mixture thereof. Pectin, gelatin and sodium carboxymethyl cellulose are among the hydrocolloids mentioned. Similarly French Patent No. 1,505,318 discloses a surgical dressing in which an adhesive comprises a viscous material and a mixture of pectin, gelatin and carboxymethylcellulose.

According to the present invention, there is provided a medically useful lyophilized sponge product having a density of 0.01 to 0.10 g/cm<sup>3</sup>, characterized in that the sponge product comprises a mixture of the hydrocolloids, gelatin, pectin and sodium carboxymethylcellulose, in the following amounts:—

20	Gelatin	20—80% by weight
	Pectin	10—50% by weight
	Sodium carboxymethylcellulose	10—50% by weight

This invention is also directed to the method of preparing this lyophilized sponge product. This method includes dry blending the gelatin, pectin, and sodium carboxymethylcellulose, adding the mixture to water with agitation so as to form a colloidal dispersion having a solids content of from 1% to 20% by weight, aerating or foaming the colloidal dispersion so that its volume increases from 10% to 600%, freezing, and then freeze drying.

The product of this invention is a white spongy foam material whose characteristics vary somewhat depending upon the composition and processing techniques. The composition and method of preparation, which are explained in detail below, permit the product to be obtained in the form of a sheet which can be sliced or cut to a desired size or milled into a granular form. The product can also be cast into discrete shapes such as cones, tampons, suppositories, etc.

The lyophilized product of this invention is capable of absorbing and holding many times its weight of whole blood or body exudates. The product is also bioabsorbable. Thus, it can be employed as a hemostatic agent to control visceral bleeding in areas of the body such as the pancreas, liver, or kidney where conventional means of control are technically impractical. The product can also be employed as an absorbable sponge in surgical procedures and for supportive surgical uses. The product can also be employed in the treatment of various open wounds such as decubitus and varicose ulcers.

The lyophilized foam product because of its hydrocolloid composition possesses wet-tack. Thus, the product can be employed as a bioabsorbable tissue adhesive for surgical procedures involving non-suturable tissue and in burn treatment and also as an adhesive in skin grafting procedures.

The solubility and absorbability of the lyophilized foam product can be reduced by cross-linking either before or after the lyophilization step. For some medical uses it may be preferable to have a partially insoluble product, for example in the adhesion of tissues, and in other medical uses a practically insoluble product may be preferred, for example when the product is shaped to be used as a colostomy plug.

As a result of the unique combination of hemostatic, adhesive, bioabsorbability, and physical characteristics of the lyophilized foam product of this invention, it can be employed in numerous medicinal and veterinary procedures.

The lyophilized foam sponge product of this invention is formed from a mixture of gelatin, pectin, and sodium carboxymethylcellulose. The pectin and sodium carboxymethylcellulose are each present at from about 10% to about 50% by weight of the final product and the gelatin is present at from about 20% to about 80% by weight of the final product. In general, as the amount of gelatin is increased the final product becomes more pliable. The foam sponge product will have a density of from about 0.01 to about 0.1 g/cm<sup>3</sup>.

Preferably the pectin and sodium carboxymethylcellulose will each be present at from about 15% to about 35% by weight of the final product and the gelatin will be present at from about 30% to about 70% by weight of the final product.

The foam sponge product of this invention may be prepared as follows. There is first formed a dry blend of gelatin, pectin, and sodium carboxymethylcellulose. Preferably, these materials are comminuted to a finely divided form so as to aid in their mixing and increase the rate at which they will hydrate. Of course, these materials as well as any of the other materials described below that may be

employed in this invention should be of a pharmaceutically acceptable purity. The dry blend is then added with agitation to water to form a colloidal dispersion. Any conventional mixing device having a propeller, gate mixer, or homomixer can be employed. The amount of water and dry blend are controlled so that the initial dispersion has a solids content of from about 1% to about 20% by weight. The density and toughness of the final product will vary depending upon the solids content and the degree of aeration or foaming. Thus, the product obtained from a colloidal dispersion having a solids content of about 1% by weight will be relatively fluffy and soft whereas a product obtained from a colloidal dispersion having a solids content of about 5% or greater aerated or foamed to the same extent will be more rigid and tough. Preferably, the colloidal dispersion contains from about 3% to about 9% by weight of the dry blend of gelatin, pectin, and sodium carboxymethylcellulose and will result in a final product having a density of from about 0.01 to about 0.03 g/cm<sup>3</sup>, depending upon the degree of aeration or foaming.

In order to obtain a uniform product, the aqueous colloidal dispersion is aerated or foamed prior to freezing. The aeration or foaming increases the volume of the dispersion to about 10% to about 600% of the original volume. The presence of gas bubbles such as air or carbon dioxide prevents or at least retards depending upon the extent of entrainment the formation of patterns in the lyophilized final product. Patterns are the result of ice crystal lattices forming in the dispersion during the freezing step and if present in the final product they are a source of nonuniformity and can cause mechanical weakness. Gas entrainment can be performed by whipping the dispersion and/or by means of a tube having a fitted cylinder that injects air or other gas into the dispersion. Dry ice can be used to generate carbon dioxide in the dispersion. Before freezing the aerated or foamed colloidal dispersion should contain from approximately 10% to about 85% by volume of entrapped gas, preferably about 60% by volume.

The foamed or aerated aqueous colloidal dispersion can be prepared at room temperature. Elevated temperatures could be employed to ensure dispersal of the hydrocolloids.

A surface tension modifier such as sodium hexametaphosphate or natural or synthetic surfactants such as lecithin and polyoxyethylene derivatives of sorbitan fatty acid esters such as Tween 60 (Trade Mark) can be added to the colloidal dispersion to stabilize the gas suspension and enhance the quality of the foam. Such agents can be added in varying amounts depending upon their surfactant ability but in general will vary from about 10% to about 100% by weight of the solids already present in the colloidal dispersion.

The foamed or aerated colloidal dispersion is then poured into metal or plastic containers and frozen. The rate of heat transfer is important since at low levels of gas entrainment, if the dispersion is frozen too slowly, the gas bubbles may rise to the surface causing nonuniformity. In order to minimize variations in the freezing step, it is preferred that small containers be employed and that freezing step be performed in a well circulated cold room that is kept at about -20°C. The frozen material is then lyophilized in a conventional freeze drying apparatus at less than about 20°C and a vacuum of about 6.67 to 20 Pa (50 to 150 μm of Hg). After drying has been completed, the foam sponge product is maintained in a dry atmosphere (relative humidity less than 50%) to prevent condensation of moisture. The foam sponge product can then be cut into the desired size, shape and thickness and hermetically sealed in a plastic bag or glass container. The packaged product can be terminally sterilized by gamma radiation of about 1.5 mega rad.

Of course, if desired, the foamed aqueous colloidal dispersion can be freeze dried in a mold tray so to obtain the final product having a particular shape. Alternatively, a granular final product can be obtained by passing the dried foam sponge product through a screen before packaging. Preferably, a number 16 mesh screen is employed so as to obtain a granular product having a particle size of less than one mm.

The lyophilized hydrocolloid foam product can be cross-linked so as to reduce its solubility and absorbability. For example, a solution of a cross-linking agent such as formaldehyde, glutaraldehyde, alum or tannin can be added to the aerated or foamed colloidal dispersion at from about 0.1% to about 10% by weight of the combined gelatin, pectin, and sodium carboxymethylcellulose. Alternatively, the product can be cross-linked after the lyophilization step by exposing the freeze dried product to formaldehyde or glutaraldehyde vapor or ultraviolet radiation. As the amount of cross-linking increases the solubility of the product decreases.

Various pharmaceutically active compounds such as antimicrobial agents can also be added to aerated or foamed colloidal dispersion. In particular, where the product is intended for use as a hemostatic agent or surgical sponge, thrombin or other hemostatically useful substances can be added directly to the aerated or foamed colloidal dispersion.

Other substances can also be added to the aerated or foamed colloidal suspension. Plasticizers such as propylene glycol or glycerine can be included within the colloidal dispersion at up to about 30% by weight of the combined gelatin, pectin, and sodium carboxymethylcellulose. The addition of a plasticizing agent will enhance the flexibility and strength of the final product.

As discussed above, the foam sponge products of this invention have a density of from about 0.01 to 0.10 g/cm<sup>3</sup>, depending upon the weight percent of gelatin, pectin, and sodium carboxymethylcellulose. The foam sponge products of this invention can absorb from about 350% to about 900% of

their own weight of heparinized whole blood and from about 700% to about 1500% of their own weight of water.

The water absorption rate of the foam sponge products of this invention are tested by placing a 1.9 cm by 1.9 cm (0.75 inch by 0.75 inch) piece on a sintered glass filter attached with a graduate pipet. The time required to have 0.05 ml of water absorbed is found to be from about 30 to 100 seconds for the foam sponge product in which no cross-linking agent is present and from about 100 to 150 seconds for the cross-linked foam sponge product.

The adhesive strength of the foam sponge products of this invention are tested by sandwiching a piece of the product between two strips of pre-soaked dialyzer tubing, 2.22 cm (0.875 inch) wide and 5.08 cm (two inches) long, loaded with a 50 g weight for three minutes. These two strips adhered by the foam sponge product are pulled apart by Chatillon gauge and at 1.2 cm/min the break point is registered. According to this procedure the break point on the Chatillon gauge is from about 400 to 900 g.

The following examples are illustrative of the invention.

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#### Example 1

A dry blend is formed consisting of 5 g of sodium carboxymethylcellulose (extra fine), 5 g of gelatin (Type A, high bloom, U.S.P. 100 mesh) and 5 g of pectin (200 mesh). The mixture is passed twice through an 80 mesh screen. This dry blend is then slowly added to 500 ml of water with vigorous agitation and a stream of air is blown into the bottom of the dispersion through a capillary tube. After approximately one hour, the colloidal dispersion becomes milky white and its volume increases to about 650 ml. The foamed dispersion is then poured into a 30 cm by 45 cm flat bottom metal tray and is frozen in a  $-20^{\circ}\text{C}$  cold room. After the dispersion is frozen solid the tray is transferred to a lyophilizer and the material is dried at  $-5^{\circ}\text{C}$  and 20 Pa (150  $\mu\text{m}$  of Hg). After about 48 hours, the material is totally dried and it is removed from the lyophilizer and sliced to the desired size. The foam sponge product is then hermetically sealed inside a plastic bag or glass container and sterilized by gamma radiation at 1.5 Mrads.

This foam sponge product has a density of  $0.04\text{ g/cm}^3$  and a pH of  $4.5 \pm 0.3$  which is determined by dissolving 0.1 g in 10 ml of water.

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#### Example 2

Sixty grams of a dry powder consisting of 30 g of gelatin (Type B, low bloom, USP 100 mesh), 15 g of sodium carboxymethylcellulose (fine) and 15 g of citrus pectin (200 mesh) is rapidly added to 1 liter of purified water with vigorous agitation such as that produced by a balloon whip. Whipping is continued for approximately 10—15 minutes or until the volume of aerating foam is approximately 3 liters. The foam is then transferred to shallow pans (e.g., 45 cm x 45 cm x 1 cm) or molds and is frozen at  $-5^{\circ}$  to  $-20^{\circ}\text{C}$  for approximately six hours. The frozen material is then lyophilized at 6.67 to 13.33 Pa (50 to 100  $\mu\text{m}$  of Hg) for approximately 36 hours at  $20^{\circ}\text{C}$ . The density of the resulting flexible foam product is  $0.02\text{ g/cm}^3$ .

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The material can be sliced into a desired size and hermetically packaged. If desired, the product can be sterilized by exposure to gamma radiation at 1.5 Mrads.

#### Example 3

Following the procedure of Example 2 but employing as the powder a mixture of 54 g of gelatin (Type A, high bloom, fine mesh), 18 g of sodium carboxymethyl cellulose (fine), and 18 g of citrus pectin (200 mesh), a foam product that is less flexible than that of Example 2 is obtained. This product has a density of about  $0.03\text{ g/cm}^3$ .

#### Example 4

Following the procedure of Example 2 but employing as the powder a mixture of 45 g of gelatin (Type A, low bloom, fine mesh), 22.5 g of sodium carboxymethylcellulose (fine), and 22.5 g of citrus pectin (200 mesh), a foam product intermediate in flexibility to those of Examples 2 and 3 is obtained. This product has a density of about  $0.03\text{ g/cm}^3$ .

#### 55 Examples 5—20

Following the procedure of Example 1 or 2 but varying the materials as set forth below additional foam sponge products within the scope of the invention are obtained.

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Ex.	Dry blend			Weight % of dry blend in the aq. dis.	Volume % of gas in the aq. dis.	Weight % plasti-cizer (glycerol) relative to dry blend in aq. dis.	
	Weight % gelatin	Weight % pectln	Weight % Na CMC				
5	5	60	20	20	6	65	—
	6	50	25	25	6	65	15
10	7	80	10	10	6	65	—
	8	70	15	15	9	50	—
15	9	60	25	15	8	60	—
	10	60	15	25	8	65	—
	11	50	30	20	9	65	—
20	12	50	20	30	9	65	—
	13	50	20	30	6	65	—
25	14	30	30	40	3	35	—
	15	40	30	30	4	40	—
	16	40	30	30	6	65	—
30	17	50	25	25	3	85	—
	18	33.3	33.3	33.4	4.5	65	30
35	19	45	30	25	7	65	—
	20	66	17	17	9	65	—

#### Example 21

Following the procedure of Example 3 but adding from about 1 to about 5 ml of formalin solution (37% by weight of formaldehyde gas in water) to the aerating foam prior to freezing and lyophilizing results in a foam that is almost completely insoluble in water.

Similarly, the aerating foams of Examples 1, 2 and 4 to 20 can be treated with formaldehyde prior to freezing and lyophilizing so as to cross-link one or more of the hydrocolloids and decrease the solubility of the final product.

Alternatively, the products of Examples 1 to 20 can be cross-linked after lyophilization by placing the product in a closed vessel for about two hours on a porous platform above a reservoir containing formalin solution. The formalin is presaturated with calcium chloride to maintain relative humidity at about 30 to 35%.

#### Example 22

Lyophilized thrombin is dispersed in a small volume of water at a concentration of approximately 10,000 units per 30 ml. This thrombin dispersion is added to the aerating foam of Example 1 and gently mixed. The thrombin containing foam is immediately frozen and then lyophilized according to the procedure of Example 1.

#### Example 23

The following *in vivo* study was performed to evaluate the hemostatic and bioabsorbability of a sponge product of this invention as compared with the commercially available product Gelfoam (Trade Mark) (Upjohn).

Twelve New Zealand White rabbits weighing approximately 2.5 kg. and having ear tags for identification were used in the study. Each rabbit was anesthetized by intravenous injection of sodium pentobarbital. The abdominal cavity was opened and the liver was exposed. An approximately 3 cm. thick slice of a lobe was incised, removed from the liver, and weighed. Immediately after incision, a piece of the sponge product prepared according to the procedure of Example 1 or Gelfoam (Trade Mark) was placed on the incisions of four rabbits each. Incisions of four additional rabbits were left uncovered

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to serve as control. The incision sites were observed for hemorrhage, and the blood loss from each animal was weighed upon clotting.

Upon cessation of bleeding, the test materials were left in place, the abdominal wall sutured, and the animals observed for survival. After ten days, all animals were necropsied, and the incision sites were examined for fate of the foam and any gross signs of tissue reaction. Mean blood loss from the group treated with the sponge product of Example 1 was compared to those of control and Gelfoam treated groups by Student's t test. Sections of liver at the incision sites were examined for histological changes.

Table 1 shows the individual weights of the blood loss and the slice of liver removed from each animal as well as their group mean values.

Incisions produced seepage of blood from the livers. The amount of blood loss was variable in the control and Gelfoam (Trade Mark) treated groups. Mean values of the blood loss were  $6.10 \pm 1.76$  g in the control,  $6.08 \pm 2.06$  g in the Gelfoam treated, and  $0.97 \pm 0.2$  g in the group treated with the product of Example 1. The difference between the control or Gelfoam (Trade Mark) groups and the group treated with the product of Example 1 was significant ( $P < 0.05$ ).

TABLE I

Group number	Rabbit number	Blood loss (g)	Liver removed (g)
I  Sponge Product of Example I	13	1.3	5.2
	14	1.0	4.3
	9	1.2	4.7
	16	0.4	5.1
	—	0.97	4.82
II  Gelfoam®	x	$\pm 0.20$	$\pm 0.21$
	I vs. III	$p < .05$	not significant
	I vs. II	$p < .05$	$p < .01$
III  Control	17	4.3	7.2
	18	2.6 (Blood collection incomplete)	5.9
	19	5.4	5.9
	20	12.0	6.5
	—	6.08	6.38
	x	$\pm 2.06$	$\pm 0.31$
	II or III	not significant	not significant
	5	10.6	4.0
	11	2.7	4.8
	1	7.1	7.3
	7	4.0	7.1
	—	6.10	5.80
	x	$\pm 1.76$	$\pm 0.83$

Table II presents the results of pathological evaluation of incision sites in the liver of each animal. No test or control animal died during the ten day observation period.

On necropsy, none of the sponge product from Example 1 was observed in the peritoneal cavity of any rabbit. Absence of this material was further confirmed on histological examination of the healed hepatic incisions. In animals treated with Gelfoam, however, the test material was still intact, grossly clearly distinguishable from the liver tissue, and adhered to the incision sites. Microscopically, it could be seen as a pink (hematoxylin-eosin-stained proteinaceous material) sponge infiltrated with blood of exudate. Gelfoam (Trade Mark) therefore, was not absorbed during the 10-day period.

Livers of all animals were found to have healed with the formation of a scar at the incision sites. Histological evaluation of the incision sites revealed proliferation of fibroblasts, formation of giant cells indicating early hepatic regeneration, and focal necrosis or suppurative inflammation in some cases. Hepatic incision sites in three of the control animals showed hemorrhages. No hemorrhages were seen in either of the treated groups. Healing of the hepatic incisions in the three groups was similar, and no tissue reaction ascribable to the test materials was observed in any animal.

Thus, under the conditions of this study, the product of Example 1 was found to have a greater hemostatic effect than Gelfoam (Trade Mark), was completely absorbed within 10 days, and elicited no tissue reaction in the peritoneal cavity.

TABLE II

Group no./animal no.	Test material	Scar	Suppuration	Giant cells	Focal necrosis	Focal hemorrhage
<b>Sponge Product of Example I</b>						
9	—	+	—	+	—	—
13	—	+	—	+	—	—
I 14	—	+	—	+	—	—
16	—	+	+	+	+	—
<b>Gelfoam (Trade Mark)</b>						
17	+	+	—	+	—	—
18	+	+	—	+	+	—
II 19	+	+	—	+	—	—
20	+	+	+	+	—	—
<b>Control</b>						
1	—	+	—	+	—	—
5	—	+	—	+	+	+
III 7	—	+	—	+	—	+
11	—	+	—	+	+	+

— =absent      + =present

## Claims

1. A medically useful lyophilised sponge product having a density of 0.01 to 0.10 g/cm<sup>3</sup>, characterized in that the sponge product comprises a mixture of the hydrocolloids, gelatin, pectin and sodium carboxymethylcellulose, in the following amounts:—

	Gelatin	20—80% by weight
	Pectin	10—50% by weight
10	Sodium carboxymethylcellulose	10—50% by weight

2. A product according to claim 1 wherein said pectin and sodium carboxymethylcellulose are each present in an amount from 15% to 35% by weight and said gelatin is present in an amount from 30% to 70% by weight.

3. A product according to claim 2 wherein said gelatin, pectin, and sodium carboxymethylcellulose are present in the same amount by weight.

4. A product according to claim 3 having a density of 0.04 g/cm<sup>3</sup>.

5. A product according to claim 2 wherein said gelatin is present in an amount of 50% by weight and said pectin and sodium carboxymethylcellulose are each present in an amount of 25% by weight.

6. A product according to claim 5 having a density of 0.02 g/cm<sup>3</sup>.

7. A product according to claim 5 having a density of 0.03 g/cm<sup>3</sup>.

8. A product according to claim 2 wherein said gelatin is present in an amount of 60% by weight and said pectin and sodium carboxymethylcellulose are each present in an amount of 20% by weight.

9. A product according to any preceding claim wherein a pharmaceutically active material is included within the sponge.

10. A product according to claim 9 wherein the pharmaceutically active material is thrombin.

11. A method of preparing a product according to any preceding claim, comprising adding a dry blend comprising a mixture of the hydrocolloids in the stated proportions, to water with agitation to form a colloidal dispersion, said dispersion having a solids content of from 1% to 20% by weight, aerating or foaming the colloidal dispersion so that its volume increases by 10% to 600%, and freezing and lyophilizing the dispersion.

## Patentansprüche

1. Gefriergetrocknetes Schwammprodukt mit einer Dichte von 0,01—0,10 g/cm<sup>3</sup> für medizinische Zwecke, dadurch gekennzeichnet, daß es ein Gemisch der Hydrokolloide, Gelatine, Pektin und Natrium-carboxymethylcellulose in folgenden Mengen enthält:

40	Gelatine	20—80 Gew.-%
	Pektin	10—50 Gew.-%
	Natrium-carboxymethylcellulose	10—50 Gew.-%

2. Produkt nach Anspruch 1, dadurch gekennzeichnet, daß das Pektin und die Natrium-carboxymethylcellulose jeweils in einer Menge von 15—35 Gew.-% vorliegen und die Gelatine in einer Menge von 30—70 Gew.-% vorliegt.

3. Produkt nach Anspruch 2, dadurch gekennzeichnet, daß Gelatine, Pektin und Natrium-carboxymethylcellulose in gleichen Gewichtsmengen vorliegen.

4. Produkt nach Anspruch 3, gekennzeichnet durch eine Dichte von 0,04 g/cm<sup>3</sup>.

5. Produkt nach Anspruch 2, dadurch gekennzeichnet, daß die Gelatine in einer Menge von 50 Gew.-% vorliegt und das Pektin und Natrium-carboxymethylcellulose jeweils in einer Menge von 25 Gew.-% vorliegen.

6. Produkt nach Anspruch 5, gekennzeichnet durch eine Dichte von 0,02 g/cm<sup>3</sup>.

7. Produkt nach Anspruch 5, gekennzeichnet durch eine Dichte von 0,03 g/cm<sup>3</sup>.

8. Produkt nach Anspruch 2, dadurch gekennzeichnet, daß die Gelatine in einer Menge von 60 Gew.-% vorliegt und das Pektin und Natrium-carboxymethylcellulose jeweils in einer Menge von 20 Gew.-% vorliegen.

9. Produkt nach einem der Ansprüche 1 bis 8, gekennzeichnet durch einen zusätzlichen Gehalt an einem pharmazeutisch aktiven Material im Schwamm.

10. Produkt nach Anspruch 9, dadurch gekennzeichnet, daß das pharmazeutisch aktive Material Thrombin ist.

11. Verfahren zur Herstellung eines Produkts nach einem der Ansprüche 1 bis 10, dadurch gekennzeichnet, daß man ein trockenes Gemisch der Hydrokolloide in den angegebenen Mengenver-



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hältnissen unter Rühren in Wasser einträgt unter Bildung einer Kolloidalen Dispersion, wobei die Dispersion ein Feststoffgehalt von 1—20 Gew.-% aufweist, die kolloidale Dispersion belüftet oder verschäumt, so daß ihr Volumen um 10—600% zunimmt, und die Dispersion gefriert und gefriertrocknet.

### 5 Revendications

1. Produit spongieux lyophilisé à usages médicaux ayant une masse volumique de 0,01 à 0,10 g/cm<sup>3</sup>, caractérisé en ce que ce produit spongieux comprend un mélange des hydrocolloïdes, gélatine, pectine et carboxyméthylcellulose sodique, dans les proportions suivantes:

10	Gélatine	20—80% en poids
	Pectine	10—50% en poids
15	Carboxyméthylcellulose sodique	10—50% en poids.

2. Produit selon la revendication 1, dans lequel ladite pectine et ladite carboxyméthylcellulose sodique sont respectivement présentes à raison de 15% à 35% en poids, et ladite gélatine est présente à raison de 30% à 70% en poids.

20 3. Produit selon la revendication 2, dans lequel ladite gélatine, ladite pectine et ladite carboxyméthylcellulose sodique sont présentes dans le même pourcentage en poids.

4. Produit selon la revendication 3, ayant une masse volumique de 0,04 g/cm<sup>3</sup>.

25 5. Produit selon la revendication 2, dans lequel ladite gélatine est présente dans une proportion de 50% en poids, et ladite pectine et ladite carboxyméthylcellulose sodique sont respectivement présentes dans une proportion de 25% en poids.

6. Produit selon la revendication 5, ayant une masse volumique de 0,02 g/cm<sup>3</sup>.

7. Produit selon la revendication 5, ayant une masse volumique de 0,03 g/cm<sup>3</sup>.

30 8. Produit selon la revendication 2, dans lequel ladite gélatine est présente dans une proportion de 60% en poids et ladite pectine et ladite carboxyméthylcellulose sodique sont respectivement présentes dans une proportion de 20% en poids.

9. Produit selon une quelconque des revendications précédentes, dans lequel l'éponge contient une substance pharmaceutiquement active.

10. Produit selon la revendication 9, dans lequel la substance pharmaceutiquement active est la thrombine.

35 11. Procédé de préparation d'un produit selon l'une quelconque des revendications précédentes, consistant à ajouter un mélange sec, comprenant un mélange des hydrocolloïdes dans les proportions indiquées, à de l'eau, avec agitation de façon à former une dispersion colloïdale, ladite dispersion ayant une teneur en solides de 1% à 20% en poids, à gazéifier ou à faire mousser la dispersion colloïdale de manière son volume augmente de 10% à 600%, et à congeler et lyophiliser la dispersion.

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